

## **REMARKS**

### **I. STATUS OF THE CLAIMS**

Claims 14-25 were pending at the time of the Action. Claim 25 has been cancelled without prejudice or disclaimer. Claims 14 and 23 have been amended. Claims 29-35 are new. Support for the amendments to the claims and the new claims can be found throughout the disclosure as well as in the originally filed claims. More particularly, support for “a nucleic acid sequence encoding the alpha subunit of the sodium channel of SEQ ID NO:67” in claims 14 and 29, can be found for example in the specification, at page 17, line 7; at page 9, line 17; at page 23, line 14; in originally filed claim 7; in the Sequence listing, as well as at page 27, line 26. Support for the mutations described in claims 14, 23, and 29 can be found in the specification, for example from page 53, line 21 to page 54, line 4; at page 27, lines 24 to 28; and at page 54, lines 9 to 10; and in Figure 7. New claims 30 and 32, and 31 and 33 are identical to claims 17 and 20 respectively, except for their dependencies. Support for new claim 34 is derived from the translation of SEQ ID NO:65, which encodes the amino acid sequence of SEQ ID NO:67. One of skill is capable of producing such a translation and identifying the initiator codon from which the amino acid of SEQ ID NO:67 is derived. No new matter has been added.

Claims 14, 17, 20, 23, 24 and 29 to 33 are now pending.

### **II. REJECTIONS UNDER 35 U.S.C. §112**

Rejection under 35 U.S.C. §112 include (A) rejection of claims 14, 17, 20, 24, and 25 due to an alleged lack of enablement, and (B) rejection of claims 14, 17, 20, 24 and 25 for an alleged lack of written description.

**A. Claims 14-25 Are Enabled by the Specification**

Claims 14, 17, 20, 24 and 25 stand rejection under 35 U.S.C. § 112, first paragraph as not complying with the enablement requirement.

Firstly, the claims are rejected based on an alleged insufficient enablement for former part (c) of claim 14. According to the Examiner, former part (c) (now part (d)) of claim 14 encompasses variants of SEQ ID NO:1 which do not encode a functional sodium channel or with any function or with no function whatsoever.

Claims 17, 20, 24 and 25 are rejected as they depend on claim 14 but claim 24 is the object of an additional rejection as it is considered as not limited to enabled embodiments. More specifically, the Examiner is of the opinion that with respect to claim 24, the specification fails to disclose to the skilled artisan the full scope of the nucleic acids which are indicative of an increased risk of epilepsy.

Applicants respectfully disagree as the claims are enabled by the specification. However, in an effort to further the prosecution of this case and secure prompt allowance, claim 14 has been amended as suggested by the Examiner to specify that the claimed nucleic acid sequence in former part (c) (now part (d)) is encoding an alpha subunit of a sodium channel. In addition, claim 14 has been modified to recite that the claimed nucleic acid comprises a specific mutation as disclosed in the instant application, thereby rendering moot the objection to claim 24. Finally, claim 25 has been cancelled.

In view of the above, the enablement rejection is moot and should be withdrawn.

For the record, Applicants note that the rejected claims are enabled and reserve the right to pursue the cancelled subject matter in further applications.

**B. Claims 14-28 Satisfy the Written Description Requirement**

Claims 14, 17, 20, 24 and 25 have been rejected under 35 USC § 112, first paragraph, as failing to comply with the written description requirement.

Specifically, the Examiner alleges that the description of the application would not reasonably convey to one skilled in the relevant art that the Applicants had possession of nucleic acids at least 95% identical to SEQ ID NO:65 or to the full length complement thereof (former claim 14, part (c)), at the time the application was filed.

In addition, claim 24 is rejected as allegedly encompassing subject matter which is not fully described by the specification. More particularly, the Action alleges that the specification fails to disclose the full genus of the claimed nucleic acid which leads to an increased risk of idiopathic generalized epilepsy.

Applicants respectfully disagree as the claims satisfy the written description requirement. However, in an effort to further the prosecution of this case and secure prompt allowance, claim 14 has been amended to indicate in amended part (d) that the nucleic acid is encoding an alpha subunit of a sodium channel (this amendment is equivalent to what has been suggested by the Examiner at page 4, lines 8-10 and at page 6, lines 13-15 of the Office Action). As indicated above, the incorporation of the specific mutations in claim 14 renders the objection to claim 24 no longer applicable and claim 25 has been cancelled. In view of the above, the written description rejection is moot and should be withdrawn.

Claim 25 stands rejected under 35 USC § 112, first paragraph as failing to comply with the written description requirement for the reasons previously made of record in the Office Action dated April 27, 2007.

Applicants respectfully disagree with the Examiner and maintain their opinion. However in an effort to further the prosecution of this case and secure prompt allowance, claim 25 has been cancelled. In addition, the mutations now recited in claims 14, 23 and 29 are described by their corresponding amino acid nature and positions with respect to SEQ ID NO:67 (corresponding to the amino acid sequence of the alpha subunit encoded by SEQ ID NO:65) which satisfies the written description requirement.

For the record, Applicants respectfully reiterate that one must not place undue emphasis on the presence or absence of literal support in the specification for the claim language. The test is whether the disclosure of the application as originally filed “reasonably conveys to the artisan that the inventor had possession at the time of the later claimed subject matter” *In re Kaslow*, 707, F.2d 1366 (Fed. Cir. 1983). Applicants maintain that support for the position of the two mutations listed in claim 25(a) and 25(b) may be inferred from the disclosure as originally filed.

Applicants would like to nevertheless submit the following clarifications as to why the specification as filed does support mutations at positions 759 to 761 and 3735 of SEQ ID NO: 65.

It is well known that cDNA not only comprises the nucleotide sequence encoding a particular protein but also comprises non-coding sequences located at the 5’ and 3’ ends of the cDNA (e.g., regulatory sequences). Thus, SEQ ID NO:65 for example comprises non-coding sequences as well as nucleotides coding for the SCN3A protein of SEQ ID NO:67.

One skilled in the art desirous of locating in SEQ ID NO:65 the nucleotide position corresponding to amino acid 43 of SEQ ID NO:67 would start by identifying the correct starting ATG (methionine) in SEQ ID NO:65. In doing so he/she would look for an ATG and subsequent nucleotide sequence that would translate into the correct amino acid sequence of SCN1A, i.e.

SEQ ID NO:67. It follows that he/she would invariably deduct that the mutation identified at amino acid 43 of the SCN3A protein corresponds to positions 759 to 761 of SEQ ID NO:65.

In addition, although the person skilled in the art would not require the following information in order to identify the correct ATG in SEQ ID NO:65, Applicants submit that SEQ ID NO:65 of the informal sequence listing originally filed had the coding sequence of its cDNA written in capital letters, thus, indicating where to find the correct first methionine ATG. Furthermore, Applicants submit that the identification of the accurate open reading frame in a nucleotide sequence could be readily completed by publicly available computer programs accessible at the priority date.

Finally, a simple computer search in SEQ ID NO:65 in "Word" format with the sequence disclosed at page 53, line 25 of the specification (CAA GAT ATT GAT GAT GAG) would allow to identify the correct nucleotide positions corresponding to the disclosed mutation. One does not need to reiterate the entire sequence for defining a specific variation can be described in the context of a smaller polynucleotide sequence.

The same reasoning applies to the G to A mutation described at position 3735 of SEQ ID NO:65, (mutation Val1035Ile of SEQ ID NO:67 or mutation in the following sequence AAA TAC RTA ATC GAT).

In view of the above, it is clear that one skilled in the art could easily infer from the specification to which portions of SEQ ID NO:65 corresponds each of the mutation described in the application.

### III. REJECTIONS UNDER 35 USC § 102

#### Claims 14-24 Are Not Anticipated by the Clare Reference

Claims 14, 17, 20 and 23-24 stand rejected as being allegedly anticipated by Clare *et al.* (Conference on Molecular and Functional Diversity of Ion Channels and Receptors, New York, NY May 14-17, 1998, published as Annals of the New York Academy of Sciences 1999, 868:80-83).

Firstly, Applicants do not agree with the Examiner's allegations that Clare *et al.* is a meeting paper that should be considered a printed article dating back to May, 1998. It is respectfully submitted that one cannot determine what was precisely presented in this poster and hence, the 1998 poster session should not be construed as a printed publication without any indication of what was disclosed therein. In the least Clare *et al.* is a 102(a) reference due to the lack of a printed publication and Applicants reserve the right to submit a declaration swearing by Clare *et al.* as a 102(a) reference.

In addition, Applicants disagree with the Examiner's anticipation allegation as the cited reference fails to disclose every element of the claims and especially, the specific SCN3A nucleic acid sequence. However, in an effort to further the prosecution of this case and secure prompt allowance, claim 14 as currently pending is directed to a purified human nucleic acid sequence comprising (i) a deletion mutation which deletes asparagine 43 of SEQ ID NO:67; or (ii) a G to A mutation which translates into an isoleucine instead of a valine at position 1035 of SEQ ID NO:67, none of which is taught or suggested by Clare.

Nevertheless, for the record, Applicants submit the following.

The Examiner states at page 9 of the Office Action:

*"The prior art is silent as to the sequence of the isolated nucleic acid, but the sequence is an inherent property. Discovering a new property, such as a sequence, of an old product does not render the product patentable (see MPEP 2112(i)). As the claim encompass a prior art product that is identical except for a feature which appears to be an inherent property, and there is no evidence of record indicating a novel and non-obvious difference between the prior art and the claimed invention, the rejection of record stands".*

According to the MPEP, paragraph 2112 in § III, it is stated:

*"Where Applicants claim a composition in terms of a function, property or characteristic and the composition of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 U.S.C. 102 and 103... This same rationale should also apply to product, apparatus and process claims claimed in terms of function, property or characteristic".*

It should be clear to the Examiner that in the present case, the currently claimed sequence is not claimed in terms of a function or property or characteristic, but in terms of structure.

In paragraph IV of the same section of the MPEP entitled "EXAMINER MUST PROVIDE RATIONALE OR EVIDENCE TENDING TO SHOW INHERENCY", it is stated:

*"The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. In re Rijckaert, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993)."*  
[emphasis **from MPEP**]

*"In re Oelrich, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981). To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient."*  
[our emphasis]

Thus, in order for a reference to anticipate a claim based on inherency, the inherency must be certain. Consequently, in the present case, it must be certain (i.e., without any doubt) that the claimed nucleic acid has the same sequence as the nucleic acid disclosed on the blot by Clare. The test is not whether there is a chance or a possibility that the nucleic acid on the blot

disclosed by Clare is the same as one of the claimed sequences. The test is whether it is certain that the nucleic acid on the blot from Clare has an identical sequence as the claimed sequence. As Clare is silent with respect to any sequence as well as any mutation present in the allegedly disclosed SCN3A nucleic acid and its relationship with epilepsy, Applicants submit that there could be no anticipation by inherency. For the record, Applicants reiterate that should the claimed sequences not comprise the specific mutations now incorporated therein, it would still be the case.

Clearly therefore, the certainty of the allegation as opposed to the possibility thereof is essential, according to case law and the MPEP, for the Examiner to establish inherency.

Still in MPEP 2112, at IV,

*"Also, "[a]n invitation to investigate is not an inherent disclosure" where a prior art reference "discloses no more than a broad genus of potential applications of its discoveries." Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings, 370 F.3d 1354, 1367, 71 USPQ2d 1081, 1091 (Fed. Cir. 2004) (explaining that "[a] prior art reference that discloses a genus still does not inherently disclose all species within that broad category" but must be examined to see if a disclosure of the claimed species has been made or whether the prior art reference merely invites further experimentation to find the species."*

Applicants respectfully submit that the teachings of Clare, are interpretable as a genus sequence. Indeed, as the claimed nucleic acid sequence of the present invention comprises 9112 nucleotides (which, as agreed by the Examiner, is not disclosed in Clare), the selection of the claimed sequence SEQ ID NO:65 comes with a probability (1 nucleotide chosen out of 4 possibilities) of 1 out of  $4^{9112}$ ! One should thus recognize that the name of the alpha subunit of the SCN3A sodium channel as Type III sodium channel, is a genus comprising an infinite number of species ( $4^{9112}$ ) one of which is selected and defined by the present invention as SEQ ID NO:65 (and SEQ ID NO:67) as well as full-length derivatives thereof that would hybridize under stringent conditions thereto.

Applicants respectfully submit that with such a complex gene and the different inconsistencies described in Clare (different sizes of mRNAs, differential splicing, “extreme” instability of the clones...[see below]), the “appearance” that the claimed alpha subunit of SCN3A is the same as that described in Clare cannot be ascertained until further undue experimentation has been carried-out and the task of sequencing this large gene has been completed. Thus, without any such indication, the Clare reference cannot be considered enabling.

Again, the Applicants respectfully submit that there cannot be an appearance that the two products are substantially identical:

- Which sequence was subcloned by Clare? Was it the 9.5 KB or the 7.5 KB sequence? It is impossible to know.
- Could it be a 6 KB cDNA, an 8 KB cDNA, a 10 KB cDNA? No one knows.
- Is it SCN3A?
- Does it comprise any of the mutations currently listed in claim 14?

Applicants stress that without any sequence whatsoever and any specific indication as to how the sequence is cloned (what fragments are used? What restriction sites? etc...), how is one skilled in the art supposed to arrive at the claimed nucleic acid molecule using the disclosure of Clare? The only information available is a band on a gel and an activity which could very well be associated to other related genes and of course nucleic acid molecules which fall outside the scope of the claims.


Finally, Clare et al., is also totally silent on the association of SCN3A and IGE and any mutation associated therewith. It is thus respectfully submitted that based on the above and the amendment to claim 14, the inherency rejection in view of Clare must be withdrawn. A request to that effect is earnestly solicited.

#### IV. CONCLUSION

Applicants believe that the present document is a full and complete response to the Action dated April 27, 2007. The present case is in condition for allowance, and such favorable action is respectfully requested.

The Examiner is invited to contact the undersigned Attorney at (512) 536-3167 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,



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Date: January 9, 2008